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# Some Epidemiological and Preventive Aspects of the Commoner Zoonoses in Canada

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## INTRODUCTION

Zoonoses are a group of communicable diseases having the following common characteristics: the disease is similar in animals and in man; the portal of entry in both man and animal is the same; the incidence in humans is highest among those in close contact with animals or animal products; and the disease is seldom transmitted from man to man.

The zoonoses have been known to man for centuries and were mentioned by Hammurabi in his Code and were discussed in the writings of Hippocrates. The World Health Organization today recognizes more than 80 diseases transmissible from animal to man. Etiologic agents of these diseases include viruses, bacteria, rickettsiae, fungi, protozoa, helminths, arthropods, and toxins. We in Canada are fortunate in that only a few of these disease problems confront us, and it is these that I propose to discuss.

The epidemiology and prevention of these diseases are of paramount concern in their control. Because of the fact that the disease is transmitted from the animal to mankind, it is axiomatic to say that control in the animal population will automatically result in its lowered incidence in man. Prevention, therefore, can be attained by control of the infection in the animal, by limiting man's contact with infected animals and animal products, and by immunization procedures in the human.

In the following discussion, I shall endeavour to group the diseases according to their etiological agents and in each group discuss those diseases which might be encountered in Canada.

## VIRUS DISEASES

### Arthropod-borne virus encephalitis

Virus encephalitis can be caused by a number of specific viruses of which Eastern and Western Equine and St. Louis types cause recognized human infection in Canada and the United States. Wild and domestic birds as well as horses serve as reservoirs of infection, and the disease is transmitted from these animals to man by the Culex mosquito. This disease occurs commonly in summer and late fall in years with high sustained temperatures.

Since arthropod-borne virus encephalitis is spread by the Culex mosquito, prevention of the disease by control of the vector is important. Such measures as proper screening of sleeping quarters, sprays, the use of repellents, and the destruction of mosquito larvae are all important measures in endemic areas. Identification of cases among horses and the identification of human cases are of epidemiological importance. Since the chief reservoir of these types of encephalitis virus is wild and domestic birds, measures to control such a reservoir of infection are

almost futile. Individual immunization of those persons at great risk with an experimental formalized vaccine has some merit, but general immunization of contacts is not an accepted procedure in a prevention program.

**Cat Scratch Fever**

Cat scratch fever is a disease which has been recognized only since 1950. The etiological agent is a virus which closely resembles the lymphogranuloma venereum and psittacosis group. Since the identification of this disease it has been reported in almost all countries in the world. Probably several animals act as reservoirs for infection of which the domestic cat is best known, transmission to humans occurring through bites, scratches, or licks from infected animals. There are no specific preventive procedures other than the avoidance of cats.

**Lymphocytic Choriomeningitis**

Although this disease is considered to be rare in humans, public health authorities agree that it is more common than the number of cases reported would indicate. For this reason it shall be considered here. This disease is caused by a filtrable virus which is capable of infecting man as well as the common house mouse. Naturally infected guinea pigs, monkeys, dogs and swine have also been observed. The virus passes from infected animals in the nasal secretions, urine, and feces, and is transmitted to man through contaminated dust and foods. In man two types of the disease exist. The disease may appear as an influenza-like infection which may either terminate in recovery or be followed in a few days by meningeal symptoms. Thus this disease presents a differential diagnostic problem in man inasmuch as it must be differentiated from other diseases causing aseptic meningitis.

Prevention of this disease centres around the control of the house mouse. Foci of infection persisting within city blocks for months or years bear testimony of the evidence of this disease in mice. General cleanliness in houses, elimination of mice and the construction of well-built mouse-proof houses are the chief methods of prevention and control of this disease.

**Psittacosis (Ornithosis)**

Psittacosis is an acute febrile disease in man caused by a virus antigenically related to that of the lymphogranuloma venereum group. The reservoir of this infection is in psittacine and ornithine birds which include birds commonly classed as pet stock, and those domestic birds such as ducks, turkeys, and chickens that are used for food purposes. The virus is transmitted to humans by cloacal discharges from birds, close contact with pet stock, or aerosol infection in poultry processing plants. Sputum from infected humans serves as an occasional source of infection.

Until 1929 this infection was regarded as rare. However, in that year a pandemic involving 800 persons of which 143 died rendered this assumption infirm. Deaths are confined to those individuals usually 30 years in age or older. In recent years the United States has loosened restrictions on the importation and marketing of imported birds with the result that human infection has risen from 25 annually in 1950 to over 300 in 1954.

One of the greatest problems in the control of this disease is its recognition and diagnosis in man. Laboratory diagnosis can be made in the first week of illness by injection of mice with sputa or blood, repeated trials often being necessary. A rise in titre of complement fixing antibody may be demonstrated, which antibody may also be found in sera of lymphogranuloma venereum infection. However, a history of contact, especially with sick birds, should make any examining physician suspicious of this disease.

Control should centre around a prevention program of strict regulation, inspec-

tion and quarantine of all imported birds, as well as quarantine and thorough disinfection of all pet shops known to have harbored the infection. The building of breeding establishments free from infection will help reduce the large reservoir of infection as will active chemotherapy of all breeding flocks. Perhaps the greatest factor in a control program is education of the public concerning the purchase of pet stock. Due enquiry should be made into the general condition of the stock in the establishment. Infected persons should be quarantined and treated with tetracycline antibiotics with a concomitant investigation of contacts and source of infection. Infected birds should be sent to the nearest laboratory for diagnosis, and carcasses should be burned after autopsy. Lastly, reciprocal respect for national methods of importation control is an important international control measure.

### Rabies (Hydrophobia)

Rabies is a disease which affects all warm blooded mammals including man and is caused by a neurotropic filtrable virus. Epidemiologists describe two disease patterns: the natural type perpetuated in wild animals such as foxes and skunks (sylvian type), and the urban type found in domesticated animals of which the canine member causes the greatest public health problem. Rabies is spread to man from the bites of infected animals and from infected Vampire bats in Central and South America. The disease does not appear in man for weeks and sometimes months after exposure to infection. Although this disease is uncommon in man, it always poses a prophylactic problem in endemic areas. Rabies has a world-wide distribution except in Australia, New Zealand, some of the Pacific Islands, Great Britain, and the Scandinavian Peninsula. Canada is an endemic area with sporadic infections of urban type rabies being reported.

Rabies is one disease in which development of clinical symptoms indicates that active treatment is hopeless; therefore, prevention is of paramount importance. Prophylactic treatment of individuals exposed to the bites of animals suspected of having rabies, with tissue vaccines, is not without danger, as severe post-vaccinal encephalitis sometimes ensues. Today investigation of an avianized live virus vaccine for human use similar to that now commonly employed in veterinary medicine is currently under way. This would greatly lessen the risk of post-vaccinal reactions. Animals suspected of having rabies or those animals having bitten humans should be held for observation for 10-14 days with subsequent autopsy and examination for Negri bodies if clinical evidence of the disease be manifest. Once a diagnosis of rabies in an animal has been made, prophylactic vaccinal therapy of individuals bitten by such an animal must be instituted. One exception to this rule should apply inasmuch as severe bites about the head and neck by animals suspected of being rabid are more dangerous than bites more distant from the central nervous system. In these individuals, it is generally felt that immediate prophylactic therapy should be instituted. Should the animal not be held for observation, prophylactic therapy should be instituted if rabies is known to exist in the area. Other methods of control are immediate destruction of domestic animals bitten by known rabid animals; preventive vaccination of dogs; education of the public in the handling and recognition of rabid animals; and co-operative programs among local veterinary associations and wild life or conservation authorities. In epidemic areas, the establishment of a control area with strict enforcement of regulations, such as the leashing of dogs, the destruction of ownerless dogs, widespread canine vaccination, and education of the public of the necessity and nature of such a control program should be immediately undertaken.

## RICKETTSIAL DISEASES

### Endemic (Murine) Typhus

Murine typhus is a rickettsial disease which is transmitted to man from infected rats by fleas. The rodent disease is naturally perpetuated by a rat-flea-rat cycle. Infected fleas, after biting man and sucking blood, defecate, thus contaminating the fresh skin wound. The infecting organism can be recovered from the rat for at least a year after exposure. This disease is world-wide in its distribution and its incidence is highest in areas such as sea ports where the rat population is high and where man and rat occupy the same buildings.

Prevention of this disease can be centred around both the control of the flea and control of the rat. Application of residual insecticide powders to rat-infected areas to control the flea population, rat-proofing buildings and the use of rat poisons are the chief means of control. Infected individuals can be treated successfully with chloramphenicol. Inoculation with inactivated *R. mooseri* vaccine may be useful in limited groups in hazardous occupations.

### Rocky Mountain Spotted Fever

Rocky Mountain Spotted Fever is caused by *R. rickettsiae* which may be found in healthy ticks (*Dermacentor andersoni*) and passed transovarially. Vertebrate hosts, such as the horse and man, are occasionally bitten by infected ticks but vertebrates are not necessary for the perpetuation of the rickettsiae in nature. This disease occurs in Western Canada and throughout most of the United States, Mexico, Colombia, and Brazil and is limited to the Western Hemisphere.

Prophylactic measures include personal prevention by avoiding tick-infected areas, careful and expedient removal of ticks from the person and by the use of insect repellents against ticks. Measures to reduce tick populations such as clearing land

and reducing small, wild animal populations are difficult and impractical. Vaccines of killed rickettsiae are especially useful in those groups subjected to high exposure. Specific therapy in infected individuals consists of the use of chloramphenicol or one of the tetracyclines.

### Q Fever

This is a rickettsial disease which is being diagnosed more frequently now than ever before, a result of a more general awareness of the disease and more efficient diagnostic criteria. Q fever is common in many countries and has been diagnosed in every continent but South America.

In man the causative ricksettiae (*Coxiella burneti*) causes an atypical type of pneumonia. It is found naturally in ticks which transmit the infective organism to sheep, goats, and cattle. Workers in slaughter houses tend to have a higher incidence of the disease because of the occupational hazard involved. The disease is commonly thought to be transmitted via the airborne route although it can be transmitted in the milk from cows with chronicly infected udders. It should be mentioned that ordinary commercial pasteurization will not destroy safely all the rickettsiae in contaminated milk.

Because of the enzootic nature of this disease with periodic explosive epidemics among those people engaged in occupations that lead to exposure, prevention is of paramount importance. An excellent vaccine prepared from *Coxiella burneti* can be used to vaccinate those in hazardous occupations. Milk should be pasteurized preferably above 62.9°C. or even boiled to assure destruction of these rickettsiae. Administration of tetracycline or chloramphenicol is specific therapy of infected individuals.

## BACTERIAL DISEASES

### Anthrax

The anthrax bacillus is capable of forming spores which are very resistant to chemical and environmental influences and which can survive for years in soil and in animal products, i.e., leather and wool. Thus, relatively permanent enzootic areas are formed which result in repeated epizootics which in turn result in heavy contamination in many parts of the world. Grazing animals infected through mucous membranes serve to perpetuate this chain. Considerable evidence now shows that anthrax can be introduced into countries by animal feeding stuffs and fertilizers contaminated in ships which have recently conveyed infected bones and hides.

The anthrax spore gains entrance to the human body through abrasions in the skin from infected animal carcasses or from contaminated fomites manufactured from infected animals such as leather products, woolen products and brushes bristled with animal hair.

Airborne infection (pulmonary anthrax) and gastrointestinal anthrax from the ingestion of infected meats are rare.

Many and diverse means are used to prevent and control anthrax. All animals suspected of having this disease should be properly treated and those dying of the disease after proper veterinary post mortem examination should be disposed of by burning or deep burial in lime pits. Excellent veterinary vaccines can be employed to control the disease in the animal population. Wastes from slaughter houses and processing plants should be controlled as well as dust control and proper ventilation in hazardous industries. Individuals employed in potentially hazardous occupations should be educated as to the danger and measures taken such as proper apparel to safeguard themselves from infection. Thorough sterilization of animal tissues prior to processing is an important domestic as well as international control measure especially in those products manufactured for export. Lastly, regulations on the importation of animal products will minimize the danger to mankind.

**Brucellosis**

Brucellosis is a disease of animal origin caused by a small gram negative bacillus. In the animal it results in abortion and for this reason is sometimes spoken of as contagious abortion. In man the disease is known also as Malta fever or undulant fever.

Brucellae are transmitted in animal populations (cattle, swine, goats) by contact with infected feces, urine, milk and tissues. Infection in man is often accidental through contact with these same infected materials, the organism gaining entrance through an abrasion in the skin. Another common source of infection is through the ingestion of unpasteurized milk. Airborne infection is rare.

Undulant fever in man is a prolonged, costly, and debilitating disease and often goes undiagnosed for considerable lengths of time. Relapses are common and may occur months or years after the initial attack. Chloramphenicol therapy is quite successful but is expensive and protracted to be effective.

Brucellosis is world-wide in distribution and is extensively found in the Mediterranean area and in North and South America. Sporadic outbreaks are seen in individuals ingesting raw milk. Diagnostic tests are sometimes difficult and for this reason a much greater number of human cases exist than are actually reported. In the United States 4000 to 5000 cases are reported annually. In France alone economic loss due to Brucellosis is estimated to be 100 million dollars annually.

Primary control of this disease lies in its control in animal populations. The search for infected animals by agglutination tests with subsequent slaughter and disposal of reactors, combined with an active calfhood vaccination program, has done much to eradicate the disease in cattle. Control in humans rests in compulsory pasteurization of milk, eradication of animal infection and the reduction of occupational hazards whenever possible.

**Erysipeloid**

Erysipeloid is a cutaneous infection caused by the organism *Erysipelothrix rhusiopathiae* which occurs throughout the world in a variety of animals, but especially in swine. Infection in man is through skin abrasions from contact with contaminated shellfish, meat or poultry. This disease resembles erysipelas in humans which is caused by hemolytic streptococci and for this reason mention is made of it here. Ultimate diagnosis rests on isolation of the organism from skin lesions.

Erysipeloid infection is readly amenable to penicillin therapy.

**Leptospirosis**

Leptospirosis infection in this country usually results from infection with either *L. icterohemorrhagica* (Weil's disease) or from *L. canicola* (infectious jaundice). Both these types of leptrospiral infections are world wide in distribution. *L. icterohemorrhagica* infects rats and *L. canicola* infects dogs, the leptospiroses being essentially animal diseases. The organisms are passed in the urine of infected animals. Human infection is accidental through contact with contaminated water or direct contact with infected animals. Infection usually results from invasion of skin abrasions or through abraded mucous membranes, although ingestion may be a mode of transmission.

Most exposed to infection are those frequently in contact with foul contaminated water, such as farmers, fresh-water fishermen, road sweepers and miners. Protection of such individuals with boots and gloves is an important preventive measure. Reducing contamination by rodent control and prophylactic vaccination of dogs in endemic areas are both good means of control. It is important in epidemics to search for the source of infection, eliminate further contamination and to prohibit further human contact with the source.

## Salmonellosis

Salmonellae organisms normally produce three types of disease in man; the "enteric fevers" which are strictly human diseases (typhoid and paratyphoid), septicemic infection due often to *S. cholerasuis,* and gastro-enteritis due to *S. typhimurium* and *S. enteritidis*, both of which may be transmitted to man from animal reservoirs. Organisms are passed from infected fowl transovarially and if eggs from such birds are not cooked adequately salmonellosis in the human may result. Feces of infected domestic fowl, household pet stock, rodents and domestic animals may contain many organisms and serve as a reservoir of infection. Usually epidemics are traced to improperly cooked meats (especially fowl), unpasteurized dairy products, insufficiently cooked eggs, and food contaminated by infected food handlers.

Salmonellosis is world-wide in distribution. Epidemics are usually seen in groups of people having a common source of food supply. Sporadic cases tend to include mild unrecognized infection.

Prevention of salmonella infection in man, therefore, stems from thorough cooking of foodstuffs (especially fowl), refrigeration of prepared food, control of salmonella infection among domestic animals, and good meat and poultry inspection with careful supervision of abattoir hygiene.

## Tuberculosis

Bovine tuberculosis is one of the chief causes of extra-pulmonary tuberculosis in mankind. The World Health Organization emphasizes the seriousness of bovine-type infection in man throughout the world and we in Canada are fortunate in that this particular hazard has been all but eradicated. Man is infected by ingestion of unpasteurized milk from tuberculous cows, by airborne infection in barns and stabling areas, and by handling contaminated animal products. Tuberculosis-free herds have also been heavily infected from attendants with open pulmonary tuberculosis caused by the bovine type of organism. Attendants infected with the human type of organism, although not causing generalized infection in cattle, may sensitize the animal to tuberculosis thus rendering inefficient one of the most important tests we have for detecting bovine tuberculosis.

In Canada the test and slaughter policy of tuberculin testing all herds with subsequent slaughter of all reactors and sanitary disposal of the carcasses has resulted in a marked reduction in the incidence of tuberculosis in cattle. Initially such a program is very expensive and for some countries economically impossible. Scandinavian countries and the United Kingdom have made very good progress with modified eradication procedures with subsequent test and slaughter methods when sufficient percentages of the animal population have been rendered tuberculin negative to make such a program economically feasible. Such programs if properly supervised are recommended by the Joint WHO/FAO Expert Group on Zoonoses.

Bovine tuberculosis is one disease that man should ultimately be able to control. Through adequate methods such as the test and slaughter program, the disease could be virtually eradicated in animal populations and hence serve as a tremendous preventive measure in the control of the incidence in man. Compulsory pasteurization of milk and dairy products and adequate meat inspection programs with condemnation of tuberculous carcasses are essential definitive measures in control of bovine tuberculosis in man. Because airborne transmission of bovine tuberculosis is possible and because infected attendants can transmit infection to tuberculosis-free herds, the World Health Organization recommends the supervision of the health of milkers and animal attendants.

### Tularemia

Tularemia is a disease caused by a small gram negative bacillus (*Pasteurella tularensis*). The disease is maintained naturally in wild animal populations as well as in some domesticated animals. Wild rodents are the chief source of infection, the infection being transmitted to man by the bites of infected flies or ticks and by inoculation of abraded skin or conjunctivae directly through handling infected animals. Hares, rabbits, and woodchucks are the main sources of the infection in man. Ingestion of insufficiently cooked rabbit meat and drinking contaminated water are also important modes of transmission.

This disease is prevalent throughout North America, the organism being named after Tulare county in California where it was first isolated. It is prevalent as well in Japan and in continental Europe. Tularemia is seen in man throughout the year, but a higher prevalence is noted in the fall as this is the season for rabbit hunting and thus there is an increased exposure rate at this time.

Prevention rests in the control of insect vectors, i.e. the Chrysops species of biting fly and the Dermacentor species of tick in areas in which tularemia is endemic. Rubber gloves should be employed by those individuals dressing wild animals or performing post mortem examination of laboratory animals. Raw water should not be consumed in areas where the disease exists. Individual treatment of infected individuals with appropriate antibiotic therapy as well as investigation of contacts and source of infection should be undertaken in each case.

## FUNGUS DISEASES

### Ringworm

Ringworm is the only zoonotic fungus disease of importance in this country and except for rare infections of epizootic lymphangitis caused by a fungus of the Blastomyces species, ringworm is the only fungus disease communicable from animal to man. The Trichophyton species of fungus is responsible for ringworm found in rural areas in association with infected cattle and horses. Infection in man caused by *Microsporon canis* occurs both in rural and urban areas wherever infected dogs or cats are present; however these cases are only sporadic in nature. The great majority of ringworm infections in man is caused by Audouini which is spread from man to man and which should be properly identified before animal sources are incriminated.

Infected individuals should undergo a regulated regimen of treatment coupled with identification of the infecting species of fungus and concomitant investigation of contacts and source of infection. In epidemic areas children before entering school should be surveyed by the Wood light. Education of the public as to the dangers of acquiring ringworm from infected animals is important in any control program. Lastly, control of animal ringworm infections per se is the most important single means of preventing spread of animal strains of ringworm fungus to humans.

## HELMINTH DISEASES

### Cysticercosis

Somatic infection with larval cysts of the pork tapeworm (*Tenia solium*) is seen in man as well as in swine. In man the eggs of the tapeworm are swallowed and hatch in the small intestine, whence the larval forms then disseminate to various tissues of the body. Very grave clinical symptoms develop when cysts develop in the central nervous system, in the heart, or in the eye. A very malignant form of this disease is basilar meningitis caused by the presence of cysticerci in the 4th ventricle.

This disease is transmitted by direct hand-to-mouth transfer of ova in feces and by contaminated food and water resulting in human ingestion and somatic infection. This infection is world-wide, occuring in those countries in which swine are raised.

Control of the animal form of the disease consists of prevention of soil pollution with human feces in rural areas, good barnyard sanitation, and education of the public. Thorough cooking of pork ensures destruction of larval forms, thus preventing the development of adult tapeworms in the intestinal tract of humans. Immediate treatment of those persons harboring adult *T. solium* is important in the control of the number of ova being passed in human excreta and hence is essential in the control of human cysticercosis.

### Echinococcosis

The Echinococcus is a genus of tapeworm which infects man only in the larval form. The common species found in Canada is that of *E. granulosus* which has in fact practically a world-wide distribution. Although infection in the white population of Canada with this organism is quite rare, it is more common in Canada's Indian population. The adult worms which are very small tapeworms, live in the intestines of dogs and related carnivora. Eggs passed in the feces of these animals are ingested by man and various wild and domestic herbivora (cattle, sheep, moose, etc.) which serve as natural intermediate hosts in which the larval form encysts. The disease is perpetuated in nature by the definite carnivorous host ingesting offal or prey infested with larval cysts.

In man the cysts may reach the size of an apple, are filled with a clear fluid, and are enclosed in a membrane. From this membrane arise buds about the size of sand grains which grow into brood capsules containing scolices. Should such cysts rupture, scolices escape, giving rise to daughter cysts. In man the liver and lungs are most commonly affected; however the spleen, kidney, heart, brain, and even bone may be affected, giving rise to a wide variety of symptoms.

Rigid control of the slaughtering of herbivorous animals so that dogs do not have access to uncooked scraps of meat is important in the control of this disease. Licensing and periodic examination of dogs with subsequent mass antihelminthic treatment have been successful in epidemics. Education of the public as to the danger and the nature of the disease is an important prophylactic consideration. Campers should always thoroughly boil water before drinking. Systematic serological examination with echinococcin and routine X-ray examination of individuals in epidemic areas, especially of those having close association with dogs, are important methods of control.

### Tape Worm

Three commonly found tapeworms infesting the intestine of man in Canada are: the beef tapeworm (*T. saginata*), the pork tapeworm (*T. solium*) and the fish tapeworm (*D. latum*). All three worms exceed six feet in length, the proglottides and ova being passed through the anus, the demonstration of which is diagnostic.

The cysts of the two tenia species are ingested with uncooked beef or pork whereas infection with *D. latum* occurs with the ingestion of raw fish. In addition to the clinical implication of infestation of the intestine with the adult worm, *T. solium* has the added hazard of causing cysticercosis.

Tapeworm infestation is world wide and where *T. solium* and *T. saginata* co-exist *T. saginata* is commoner. *D. latum* infection is especially common among the Indian and Eskimo populations of Canada because of the quantities of uncooked fish consumed.

Prevention consists of thoroughly cooking pork, beef and fish to destroy all larval forms. Because the ova passed from infected individuals are capable of infecting the respective animal host, safe sanitary disposal of all human excreta is of paramount importance in control of tapeworm infestation.

### Trichinosis

The trichina or *Trichinella spiralis* thrive in many different mammals, the source of infection in man however being almost always pork. The adult worms do not pass in the feces but become embedded in the intestinal mucosa often forming a catarrhal inflammation. Larval forms find their way into the blood stream and thence into skeletal muscle where they become encapsulated and can live in this state for ten or more years.

This disease can be perpetuated in nature by the consumption of uncooked infected mammalian flesh. In countries where all slaughtered pigs are subject to microscopic examination, trichinosis is rare in man but still persists in wild carnivorous animals. Swine readily become infected by ingesting infected rats and mice and by feeding on uncooked meat scraps and garbage.

Since swine are the chief source of human infection, prevention of the disease in swine is important in its control in man. Farmers should be encouraged to use good sanitary practices such as adequate disposal of swine and rat carcasses and the cooking of all garbage and offal fed to swine. Local and federal meat inspection and adequate processing of pork products would greatly reduce the incidence of trichinosis in man. Finally, thorough cooking of all pork products for human consumption is the surest method of preventing human infection.

## SUMMARY

In the foregoing, some of the epidemiological and preventive aspects of the zoonoses common to Canada have been briefly presented. Many zoonoses exist throughout the world of which no mention has been made but which in this day of modern transportation might possibly be encountered at any time in this country.

The following chart will serve to summarize the disease processes mentioned.

| *Disease* | *Vector* | *Portal of Entry* |
|---|---|---|
| Arthropod-borne encephalitis | Birds, Equines, Mosquitoes | Skin (mosquito bite) |
| Cat scratch fever | Cats | Skin |
| Lymphocytic Choriomeningitis | House mouse | Respiratory and digestive tracts |
| Psittacosis (Ornithosis) | Psittacine and ornithine birds | Respiratory tract |
| Rabies | All mammals | Skin (bites, abrasions) |
| Endemic (Murine) Typhus | Rat; flea | Skin (flea bite) |
| Rocky Mountain Spotted Fever | Tick (Dermacentor sp.) | Skin (bite) |
| Q Fever | Ticks, sheep, goats, cattle | Respiratory tract |
| Anthrax | Herbivores | Skin (puncture wounds) |
| Brucellosis | Cattle, swine, goats | Skin, digestive tract |
| Erysipeloid | Swine | Skin |
| Leptospirosis | Rats, dogs | Skin, digestive tract |
| Salmonellosis | Fowl, cattle, dogs, cats | Digestive tract |
| Tuberculosis (Bovine) | Cattle | Digestive and respiratory tracts |
| Tularemia | Ticks, flies, rodents | Skin, respiratory and digestive tracts |
| Ringworm | Dogs, cats, cattle, horses | Skin |
| Cysticercosis | Swine | Digestive tract |
| Tapeworm | Cattle, swine, fish | Digestive tract |
| Trichinosis | Swine | Digestive tract |
| Echinococcosis | Dog, domestic and wild herbivores | Digestive tract |

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## THE PLACE OF MANIPULATIVE TREATMENT IN LESIONS OF THE LUMBAR SPINE

D. R. L. Newton, Post. Grad. Med. J., 34: 378-382, 1958.

Manipulative treatment of lesions of the lumbar spine is empirical and is regarded as a form of quackery by many medical men. It must be remembered, however, that traction of any type is just another form of manipulation.

Three results may be achieved from the use of manipulation.

1. Adhesions can be broken down.
2. Contracted joint capsules can be stretched.
3. Displaced structures can be replaced.

Audible clicks and a sense of well being usually accompany manipulation of the normal spine. The same effects are experienced by those who stretch, producing flexion of the spine when overtired or upon waking in the morning.

Manipulation has come into dispute because it is most often applied by someone quite ignorant of the pathological process underway or else no thought has been given to the etiological factors.

The absolute contra-indications to manipulation are neoplasms, intra-spinal tumors, myelomatosis, Paget's disease, osteomyelitis, osteoporosis and fractures.

The entities which in the past have been treated with manipulation include sacro-iliac strain, lumbo-sacral strain, prolapsed intervertebral disc, post-traumatic adhesions, strained ligaments and muscles, nipped synovial fringe and facet syndrome. These of course may all produce the same symptoms at any time during their course and the conclusion is reached that the manipulation should be discontinued if it increases the severity of the symptoms. In any form of treatment, one cannot be too careful, and it must be remembered that the method is non-specific and the preoccupation with the necessity of putting something back is liable to lead to over-treatment.

The techniques of manipulation should be learned from an experienced tutor because various methods achieve equally good and equally bad results when used by different people.

—Glenn Oliver, '60

# Current Concepts of Anticoagulant Therapy

WILLIAM MANAX, '59

## INTRODUCTION

One of the striking developments in therapeutics in the last ten years is the introduction of anticoagulant therapy, now used in a great variety of intravascular clotting, both arterial and venous.

Besides abnormalities in the clotting mechanism, other factors such as venous stasis, prolonged immobilization, and pathological changes in vessel walls call for consideration. At present, the most promising line of treatment in many cases is the use of anticoagulant drugs, provided this is adequately controlled.

## HISTORY

The anticoagulants in common use fall into two main groups, distinct in respect to chemistry, mode of action, administration, and methods of control. They are

1. heparin and its analogues
2. the coumarin derivatives.

As late as 1934 surgery was helpless against thrombosis. Heparin was discovered by McLean in 1916. In 1933, Best and his co-workers solved the problem of preparing large quantities of heparin. Between 1935 and 1942, Gordon Murray in Canada and Crafoord in Sweden simultaneously and independently showed that thrombosis can be prevented by heparin post-operatively. Dicumarol was described, isolated, and synthesized by Link in 1940, and came into clinical use in 1941. The discovery of this agent is attributed to Schofield in 1922.

## HEPARIN AND ITS ANALOGUES

### 1. Origin and Action

These are polysaccharides of high molecular weight. Heparin is a naturally occurring anticoagulant which comes from mast cells. The key to the physiologic activity of heparin appears to be its strongly acidic property by means of which it forms stable salts with many proteins (Comroe and Schmidt, 1943). If the protein has enzymic or other biologic properties, heparin may be expected to enhance or inhibit these. The anticoagulant property of heparin appears therefore to depend upon a protein, a co-factor, present in plasma. Jaques in 1943 found the following relationship between heparin and certain proteins, such as casein and protamine.

$$\text{Protein} + \text{heparin} = \text{protein} - \text{heparin}$$
$$(\text{protein}) \times (\text{heparin})$$
$$(\text{protein} - \text{heparin})$$

It has been postulated that the co-factor mentioned above is a fraction of serum albumin.

Brinkhaus (1939) demonstrated that heparin, in the presence of blood serum antagonized the activation of prothrombin to thrombin. This action of heparin prolongs the clotting time of blood. The activity appears to be proportional to the amount present in the circulating blood. However, the action ceases when enzymic

destruction of heparin occurs. The action of heparin on prothrombin in the presence of blood is immediate. It does not, however, retard the formation of prothrombin by the liver.

### 2. Safety Factor

Heparin is relatively safe even when given in excessive amounts, because its effect can be rapidly overcome with protamine sulfate, and because of the short duration of its action, but this latter effect is also a disadvantage as it entails repeated intravenous administration.

### 3. Administration and Dosage

Unfortunately, heparin is effective only when given parenterally. There are two methods of administration.

a) *Intermittent Intravenous Injections*

This is the method most used in Britain, and consists of intermittent intravenous injections of 50 mg. every four hours, the aim being to keep the blood clotting time twice to three times that of the control. With this regime, wide fluctuations in clotting time occur, but in practice the method has been found satisfactory in the great majority of patients. Intramuscular injections of heparin are less certain in effect than when given intravenously, and often gave rise to pain and local bleeding into the tissues. Therefore the latter ought to be used only when intravenous injections are impossible.

b) *Intravenous Continuous Method*

Some observers feel that heparin is best given clinically by means of a continuous intravenous drip transfusion, the amount administered being adjusted to maintain the desired level of blood clotting time. This method often proves difficult when utilizing an I.V. infusion. It must also be carefully remembered that if heart disease is involved in the particular case, care must be taken not to overload the circulation. The dosage for this method is 250 mg. per day, on the average.

### 4. Advantages and Disadvantages

Intravenous heparin is the most certain and effective anticoagulant, and should always be used initially when there is an urgent indication for treatment. It acts within 5 minutes intravenously. Long-continued administration is unnecessary and undesirable, because of the expense of the drug and the necessity for its intravenous injection, and treatment can be continued with one of the coumarin drugs. Dangerous bleeding is rare, and when it occurs, hematuria is usually the first sign.

### 5. Treatment of Overdosage

Protamine sulfate removes in seconds to minutes the interference by heparin with the clotting mechanism. To eliminate completely the heparin effect, administer protamine sulfate, mg. for mg. of heparin given during the immediate past four hours. To simply lessen the heparin effect, a smaller dosage than that above should be utilized, the amount depending on the clotting time desired. It is important to remember always that elimination of the anticoagulant effect may lead to recurrence of the problem for which it was given. So modification is usually what is desired.

### 6. Analogues

Other substances, with the same action as heparin, but cheaper and easier to prepare, are at present under trial in various centres. Dextran sulfate is the most promising of these synthetic analogues of heparin.

## COUMARIN ANTICOAGULANTS

Prominent in this group is bishydroxycoumarin (Dicumarol). The main coumarin derivatives we hear about today are ethyl biscoumacetate (Tromexan), warfarin (Coumadin), Sintrom, and phenindione (Dindevan, Hedulin, Danilone).

The following discussion will mainly relate to Dicumarol.

**1. Origin and Action**

Dicumarol is related chemically to the naphthoquinone derivatives with vitamin K activity. Because of this chemical resemblance, Dicumarol acts as an anti-Vitamin-K by the method of substrate competition. In the liver, Dicumarol replaces Vitamin K at its normal site of action, and prevents its normal physiological function, and prothrombin production is depressed. As the syndrome of Vitamin K deficiency develops, the plasma prothrombin level fails, and blood coagulability is depressed. The effect of Dicumarol on the clotting time of blood occurs only in vivo.

**2. Toxicologic Effects of Dicumarol**

The principal toxic effects of this drug relate to hemorrhagic manifestations. Experimentally in rats, Rose, Harris and Chen (1942) showed central necrosis of the liver resulted from repeated large doses. However, in therapeutically effective doses of the drug clinically, there has been no evidence of change in blood picture, blood chemistry, renal fuunction tests or liver function tests.

**3. Administration and Dosage**

This is inexpensive, but takes longer to affect the clotting mechanism than heparin. One controls the use and dosage of Dicumarol by the patient's prothrombin time. Dicumarol should be administered only when facilities are available to check repeatedly the prothrombin time of the patient's blood. Probably the best procedure used for routine prothrombin determinations is the Quick Method, the details of which need not be discussed in this article.

A generally accepted schedule for the administration of Dicumarol is as follows:

i) First day, check the prothrombin time. (Control of time at Victoria Hospital, London, Ont., is 20 seconds.)

ii) Day I - 300 mg. Dicumarol orally, if prothrombin time is normal. (20 seconds or less)

iii) Day II - check the prothrombin time, and convert into percentage of prothrombin activity. Only if the prothrombin activity is more than 25%, should an additional 200 mg. be administered.

iv) Day III and subsequent days - the prothrombin time should be checked and charted. The following chart may be utilized.

| *Prothrombin Time* | *Amount of Dicumarol to be Administered* |
|---|---|
| 20 sec. | 100 mg. |
| 30 sec. | 75-100 mg. |
| 40 sec. | 50 mg. |
| or over 40 | 0-50 mg. |

It generally requires three days for Dicumarol to increase the prothrombin time appreciably.

**4. Advantages and Disadvantages**

Dicumarol is inexpensive, and can be given orally. With accurate prothrombin time estimations, the dosage of Dicumarol is fairly easily controlled. It is slow in taking action, but this deficit is compensated by the initial use of heparin. Its toxic effects are not a serious problem.

**5. Treatment of Overdosage**

Again, with the coumarin derivatives, modification rather than elimination of the coumarin effect is desirable. Therefore, the dosage of the antidotes, namely Vitamin K, or Vitamin $K_1$ oxide could be as little as 5 to 10 mg. per os (tablet form) or 50 to 75 mg. or even more intravenously, repeated if necessary. Ordinarily, the full effect of the material administered is obtained within four hours, but this is dependent on the ability of the liver to use K, or $K_1$ oxide as a precursor of prothrombin. If liver function is poor, a much greater dose of these antidotes may be required, even up to 400 to 500 mg. intravenously. Also, longer than normal time for action of these may occur in the presence of poor liver function.

## INDICATIONS TO THE USE OF ANTICOAGULANTS

### I. Thrombophlebitis in Lower Extremities

(With or without pulmonary embolism)

Thrombosis in the veins of the lower extremity may give rise to emboli, which may proceed via venous circulation to the lungs, there becoming a pulmonary embolus, with a subsequent possibility of a pulmonary infarction. Anticoagulants have little effect on the existing thrombi, but should be used to prevent propagation.

### II. Cardiac Affections

1. *Coronary Thrombosis*

Not all cardiologists are agreed that anticoagulants should be employed in the treatment of acute coronary thrombosis. Samuel Levine of Boston feels that anticoagulant therapy should be given in all cases of coronary thrombosis in which the diagnosis is definite, either mild or severe, if there are no contra-indications, and facilities for determining the prothrombin time are reliable. Anticoagulants here have a threefold action. (a) They prevent the occurrence of a mural thrombus, which in turn may be a source of embolus. (b) They prevent retrograde spread of the thrombotic process, lessening the progression of infarction. (c3 They reduce the possibility of venous thrombosis in the veins of the lower extremities.

2. *Prolonged Auricular Fibrillation*

This may give rise to an auricular thrombus, which once again may serve as an embolic source. The two commonest causes of auricular fibrillation are (a) mitral stenosis, (b) thyrotoxic heart disease.

3. *Arteriosclerotic Heart Disease*

Theoretically, the use of anticooagulants in occlusive arteriosclerotic lesions should help prevent the extension of thrombosis. Some observers feel anticoagulants do not help to any great degree in this matter.

4. *Subacute Bacterial Endocarditis*

The administration of anticoagulants here again is controversial. The embolic phenomenon is a well-established pathological finding in many cases of subacute bacterial endocarditis. However, it is also well-recognized that patients with this disease have a tendency to bleed, commonly manifested by petechiae, hematuria, etc.

### III. Cerebrovascular Accidents

Anticoagulation, if used here, is given early in the treatment. The administration of heparin to correct sludging of the blood or to prevent further vascular lesions has been advised to some authors. Although there are no data to prove the value of anticoagulant therapy, Dicumarol should be given to patients in whom the diagnosis of cerebral thrombosis can be established with reasonable certainty. This therapy will probably kill a person if misdiagnosis has been made, and a cerebral hemorrhage present. It must also be borne in mind that a cerebral thrombosis may have a hemorrhage in association with it.

Most authorities presently agree that patients with central retinal artery or vein thrombosis should be anticoagulated.

### IV. Peripheral Vascular Diseases.

1. *Thromboangiitis Obliterans (Buerger's Disease)*

This is a disease characterized by structural changes in the peripheral arteries, veins and nerves, with associated venous and arterial thrombosis frequently leading to gangrene. Anticoagulants may be used here to combat the progressive thrombosis which frequently results in arterial occlusion so severe as to necessitate amputation.

2. *Atherosclerosis of peripheral vessels is a doubtful indication.*

3. *Raynaud's Disease also presents controversy.*

4. *Arterial Embolism and Thrombosis*

Sudden occlusion of a systemic artery by a thrombus or an embolus causes an immediate ischemia of the tissues in the area supplied and secondary vasospasm of arteries in the involved region or extremity, further reducing the blood supply. If the embolus is large, involving a major vessel high in the extremity, embolectomy is indicated. Anticoagulants should be used following embolectomy until there is no further danger that clotting will occur at the site of the operation.

It should be mentioned now that long term therapy in peripheral vascular disease is still being investigated. Although the use of anticoagulation in various disease processes is a subject well open to controversy and argument, it can be stated with some assurance now that it is absolutely indicated in the following:

1). thrombophlebitis

2). pulmonary embolism

3). acute coronary thrombosis

## CONTRAINDICATIONS TO THE USE OF ANTICOAGULANTS

1. Any hemorrhagic tendency, whether from primary disease of the blood or blood vessels such as hemophilia and purpura, or from vitamin C or vitamin K deficiency. The possibility of hypoprothrombinemia and the consequent danger of bleeding should be remembered particularly in patients with obstructive jaundice of intestinal malabsorption (from vitamin K deficiency) and also in patients with hepatic cirrhosis.

2. Ulcers, benign or malignant, in any site, but particularly in the alimentary and urinary tracts. Recent gastric or duodenal ulceration makes anticoagulant therapy very hazardous.

3. Recent trauma to the brain or spinal cord. Destructive hemorrhage from anticoagulants is especially likely in such lesions, which may even include recent cerebral embolism or thrombosis.

4. Severe renal insufficiency, in which the potential toxicity of anticoagulants is increased by their accumulation in the body, making great caution necessary in their use.

5. Pregnancy—a relative contraindication.

6. Be hesitant in using anticoagulation as therapy in congestive cardiac failure. The value of these agents in the prevention of thromboembolism during congestive heart failure is under investigation.

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# Disturbances of Cardiac Impulse Formation

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## INTRODUCTION

The arrhythmias are described as variations in cardiac rate and rhythm. Causes may be pathologic or physiologic changes in the regulators of the heart beat, in the conduction apparatus or in the ability of some part of the heart to respond to stimulation. This review concentrates on the disturbances in cardiac impulse formation, and does not include the various heart blocks. The causative mechanism, the pertinent electrocardiogram (ECG) findings, the etiologic agents, the signs and symptoms, and the treatment are presented. The following review is based on Friedberg's classification.

## A. SINO-AURICULAR RHYTHMS

### I. With Abnormal Rate

1. *Sinus Tachycardia*

In sinus tachycardia there is a regular sinus rhythm at a rate varying from 100 to 160 per minute. The etiology is vagal depression and accelerator stimulation in varied degrees. Physiological stimulation results from emotion, exercise, and digestive disturbances. Pathological causes are hyperthyroidism, anemia, fever, shock, hemorrhage, congestive heart failure, and cardiac neuroses.

The patient may be asymptomatic, or may complain of disagreeable palpitation, fatigue, and restlessness. Physical examination reveals a rate of 100 to 160 per minute, increasing with exercise, and decreasing with rest.

Treatment is directed toward the underlying cause. Occasionally a persistent tachycardia disappears only after tobacco, alcohol or the excessive use of coffee is eliminated.

2. *Sinus Bradycardia*

This consists of a regular sinus rhythm at a rate less than 50 per minute. The mechanism is probably an increase in vagal tone, or a decrease in sympathetic tone. The electrocardiogram draws a PR interval of one second or more with complete regularity.

Sinus bradycardia may normally occur in sleep, pregnancy, or good physical condition as seen in athletes or those engaged in strenuous labor. Under pathological conditions it may be associated with cerebral lesions, increased intracranial pressure, coronary heart disease, convalescence from infectious disease, myxedema, icterus, and in patients treated with ACTH or cortisone.

Patients are usually asymptomatic but dyspnea, palpitation, precordial pain, dizziness, or syncope may occur. On physical examination, the pulse rate is below 50 per minute. It is completely regular. The rate is increased with exercise and decreased with rest.

Usually no treatment is necessary.

### II. With Irregular Sequence of Impulse Formation

1. *Sinus Arrhythmia*

In sinus arrhythmia the cardiac impulses arise normally, but their rhythmicity varies. This variation is thought to be

merely a physiologic variation with respiration. On ECG the PR intervals consist of a series of longer and shorter cycles.

Sinus arrhythmia is common in children and the aged. It is especially noted with bradycardia. It is often observed with rheumatic fever, following digitalization, convalescence from infectious diseases, and in diseases of the brain with increased intra-cranial pressure.

As a rule it is asymptomatic. It is of no clinical importance and requires no treatment.

2. *Sinus Arrest and Atrial Standstill*

Sinus arrest and atrial standstill is a standstill in the entire heart due to a momentary failure of the sinus node to initiate an impulse. It may occur for a period of one cycle or longer.

The mechanism is thought to be either a reflex vagal stimulation through the carotid sinus, or a direct stimulus of the vagal centre.

It is usually of no clinical significance unless the pause is excessively prolonged. Dizziness, faintness, and syncope may ensue. It is noted clinically by a dropped beat heard over the apex or felt at the wrist. It must be differentiated from the dropped beats of partial heart block, and the compensatory pause following an early premature beat.

Atrial standstill denotes a pause in atrial contraction, while the ventricle contracts in response to stimulation by its own pacemaker. The cause is usually digitalis or quinidine intoxication, but organic heart disease is often present. Treatment is removal of the causative drugs. An ECG is essential for the diagnosis.

## B. ECTOPIC BEATS AND ECTOPIC RHYTHMS

### I. Escape Rhythm

Escape rhythms are initiated by lower centres when the sinoatrial node (SA) fails to initiate an impulse, when its rhythmicity is depressed, or when the impulses are blocked.

1. Nodal rhythm occurs when the impulse arises in the atrioventricular (AV) node. The rate is usually slowed. When the AV node controls isolated beats, and the SA node controls the remainder, it is called a wandering pacemaker.

Nodal rhythm can be seen on ECG by normal and regular sequence of the QRS complex. The rate is 40 to 50 per minute.

Clinically nodal rhythm is seen in the diseased heart. Conditions are hypertension, coronary heart disease, elderly persons with high vagal tone, acute coronary occlusion, various infective diseases, and after atrial flutter. Occasionally disturbing palpitation, or choking sensation may be present. Diagnosis is established by the ECG.

Treatment is either directed toward the underlying disease or toward the removal of the causative agent, such as digitalis. Nodal rhythm can be abolished by atropine or exercise.

2. AV rhythm with reciprocal beats occurs when the AV nodal impulses pass retrogradely to activate the atria, which may then cause an SA impulse.

3. When the AV nodal rhythm does not pass retrogradely, the SA node may still activate the atria, while the AV node activates the ventricles. This is called AV rhythm and AV dissociation.

4. In cases of AV rhythm and dissociation, an occasional sinus impulse may activate both atria and ventricles interfering with nodal rhythm. This is called interference dissociation.

5. Idioventricular rhythm occurs when both the SA node, and the AV node are depressed. The impulses arise from still lower centres which may be either in the AV bundle or in the specific tissue.

The latter four are variations of nodal rhythm. The diagnosis is established by ECG. Treatment is basically the same as nodal rhythm.

### II. Premature Contractions (Extrasystoles)

The heart rhythm is interrupted by an activating impulse from a focus outside the SA node. The beats may occur regularly or irregularly. An example of the latter is the coupling seen with digitalis intoxication. The point of origin may be atrial, AV nodal, unknown supraventricular, or ventricular.

These beats occur when an ectopic focus becomes so irritable that its rate of impulse formation exceeds that of the SA node. There is also some evidence that higher centers such as the hypothalmus and cortex control the spinal sympathetic accelerator centers. Drugs such as epinephrine, ephedrine, digitalis, and barium chloride may cause extrasystoles.

The majority of patients have no heart disease. Yet the presence of heart disease tends to increase the occurrence and frequency of premature beats.

Atrial premature beats tend to occur in association with enlargement of the atria as seen in mitral stenosis or cor pulmonale. Their occurrence may also be related to emotional stress, mental or physical fatigue, irregular sleep, excessive use of alcohol, coffee, or tobacco.

Clinically the patient may be asymptomatic or he may have sensation of stoppage of the heart, dizziness, faintness, and intense anxiety. When the beats recur frequently, symptoms such as impending death, intense anxiety, pallor, sweating, nausea, and faintness may occur. On auscultation, it is recognized by a beat which occurs before the expected next normal beat. It is followed by a longer pause than normal. It must be differentiated from atrial fibrillation, and sinus arrhythmia and heart block. The diagnosis is made by the ECG.

The asymptomatic patient usually requires no treatment. When the symptoms are distressing, reassurance should be given that there is no underlying heart disease. It may be recommended to the patient that adequate sleep, periods of relaxation, a bland diet, and good mental hygiene are necessary.

Drugs found to be useful are procaine amide, quinidine sulfate, and potassium salts. Procaine amide is given orally. The initial dose is 0.75-1.25 gm. followed by 0.5 gm. three or four times daily. The maintenance dose is 0.25 gm. four times a day. Toxic effects, such as agranulocytosis, are seen with doses greater than 4.0 gm. daily.

Quinidine sulfate may also be used. The initial dose is 0.2 gm. followed by 0.3-0.6 gm. three to six times daily for a trial period of one week. Maintenance dose should be determined by gradual reduction.

Potassium salts may be effective, especially when premature beats are due to digitalis toxicity. Dosage is 2-4 gm. three or four times daily dissolved in 25% solution and suitably flavored. It may also be given in tablet form. For intravenous use 50 mEq. dissolved in 500-1000 cc of 5% dextrose and water may be given over a period of two hours.

### III. Ectopic Tachycardias

1. *Atrial Paroxysmal Tachycardia*

Atrial paroxysmal tachycardia consists of a rapid and regular succession of ectopic beats arising in the atrium which occur in paroxysms of varying duration. The beginning and ending of attacks are abrupt. The rate varies from 140 to 220 per minute but most commonly is 180 to 200 per minute. The ventricles respond in a 1:1 ratio.

Predisposing causes are nervous, toxic, and digestive disturbances.

A sudden onset without warning is characteristic. There is a continuous pal-

pitation, fluttering, or racing of the heart beat. Occasionally there may be precordial pain, a smothering sensation, or a sense of pulsation in the neck. Anxiety, weakness, exhaustion, coldness or sweating may be present. If the paroxysm is prolonged, serious circulatory disturbances may develop. The usual duration is a few minutes to a few hours.

Physical examination reveals a rapid heart rate, usually exceeding 150 beats per minute, and remaining constant despite changes in position, emotion, or exercise. The ECG shows a rapid regular series of QRS complexes. The T wave is fused with the P wave.

Treatment consists of first attempting the simple procedures which will cause vagal stimulation, such as sitting with the head between the knees, holding a deep breath with the glottis closed, induced gagging and vomiting, painful pressure on one eyeball, or caroted sinus stimulation for 10 to 30 seconds.

When the simple procedures are unsuccessful, drug therapy may be useful in an attempt to revert the tachycardia. Lanatoside C given intravenously is now widely accepted as the drug of choice. Dosage schedule is 0.8 mg. repeated in 30-60 minutes if necessary.

Ouabain can be used, but on occasion causes fatal tachycardia. Dosage is 0.5 mg. diluted in 20 cc. of physiologic saline given intravenously over a 5 minute period. Additional doses of 0.1 mg. half hourly may be necessary.

Other drugs found useful but not as effective are neo-synephrine, methoxamine mecholyl, procaine amide, and quinidine.

For the prevention of frequently occurring attacks, a daily maintenance dose of oral digitalis preparation may be necessary. Quinidine is also effective.

2. *Atrial Flutter*

A rapid co-ordinated contraction of atrial muscle with rates between 200-350 per minute constitutes atrial flutter. The ventricular rate is commonly one half the atrial rate, but may be one third or one quarter, depending on AV conduction.

The mechanism is theorized to be either a circus movement or repetitive stimuli from an ectopic focus in the atrium. Atrial flutter is observed more commonly with heart disease, especially with rheumatic heart disease and mitral stenosis. It may also be associated with hyperthyroidism, coronary and hypertensive heart disease.

The patient presents with palpitation, anxiety, weakness, dizziness or syncope. Signs of congestive heart failure may be present. Upon physical examination, the heart rate is found to be rapid and regular. It does not alter with position or exercise. Carotid sinus massage will slow the rate in a jerky, irregular fashion as the AV block is increased by vagal stimulation. Duration of an attack may last from days to months to years. This is a differentiating point to distinguish it from paroxysmal tachycardia.

The ECG shows the P waves as absolutely regular. They may be oscillations resembling saw teeth, called "f" waves. The P-R interval is prolonged. The QRS complexes commonly follow every second P wave.

The principle of therapy is to slow the ventricular response, so that congestive failure will not occur. This is followed by an attempt to convert to normal sinus rhythm.

Digitalis is the drug of choice for the slowing of ventricular rate. The dosage schedule will be discussed under atrial fibrillation. The initial digitalization dose may convert either to normal sinus rhythm, or to atrial fibrillation. If the latter occurs, quinidine may be used in an attempt to convert to normal sinus rhythm.

If no conversion is affected, the patient should be maintained on digitalis with an AV rate of 70-90 per minute.

3. *Atrial Fibrillation*

Atrial fibrillation is an uncoordinated irregular beating of the atria, the major muscular movements usually occurring at a rate of 350-500 per minute. The ventricles respond irregularly, the rate depending on AV conduction. The ventricular rate is generally from 90 to 160 per minute. It may be either transient or persistent.

The mechanism is thought to be the same as that causing atrial flutter, namely either a circus movement or rapid discharges from one or more ectopic foci.

Fibrillation is commonly seen in cases of rheumatic heart disease, mitral stenosis, coronary heart disease with heart failure, hyperthyroidism, and following acute myocardial infarction. It occasionally is seen in normal hearts especially following thoracic surgery, pneumonia, after burns, or with renal or biliary colic. In some cases tobacco, alcohol or coffee seem to be the precipitating cause.

The patient complains of palpitation, pre-cordial oppression, or pain, anxiety, weakness, and dizziness. Signs and symptoms of congestive heart failure may develop. Another complication is atrial thrombosis with cerebral, peripheral or visceral embolization or infarction.

On physical examination, the apex beat is completely irregular with a rate of 100-140 per minute. Often a pulse deficit is noted between the apex beat and the radial pulse. On auscultation, the second sound may be absent. The first sound varies in intensity. Exercise increases the rate while vagal stimulation will decrease it. Other signs depend on the underlying cardiac disease.

The ECG reveals a replacement of the P waves by "f" waves. The QRS complexes are irregularly spaced.

Paroxysms usually last for several hours or occasionally for a few days. If they persist for greater than two weeks, they are usually permanent. The latter is an unfavorable prognostic sign as congestive failure is impending, if not already established. The former occurrence is also serious especially in a diseased heart because of the greater probability of failure or embolization.

Treatment depends upon whether heart disease is present or not. When it is present, digitalis is the drug of choice. Where it is absent, quinidine is indicated.

In digitalis therapy, the choice of preparation depends upon the speed of digitalization desired. In the following table is given the initial and maintenance dose of the more common preparations.

(a) *Oral Administration*

| | Digitalizing Dose | | |
|---|---|---|---|
| | Average | Range | Maintenance Dose |
| Digitalis Leaf | 1.8 gm. | 1.2 - 2.0 gm. | 0.1 gm. |
| Tincture of Digitalis | 18.0 cc. | 12 - 20 cc. | 1.0 cc. |
| Digitoxin | 1.8 mg. | 1.2 - 2.0 mg. | 0.1 mg. |
| Digoxin | 3.75 mg. | 2.0 - 5.0 mg. | 0.25 mg. |
| Gitalin | 5.5 mg. | 3.0 - 10.5 mg. | 0.5 mg. |
| Lanatoside C | 7.5 mg. | 5.0 - 10 mg. | 1.0 mg. |

If the patient has received digitalis within the past two weeks, digitalis leaf 0.1 gm. every 6 hours should be given. The patient should be observed carefully for therapeutic or toxic effects. Favorable effects are a ventricular rate of 70 to 80 and a disappearance of the pulse deficit.

(b) *Intravenous Administration*

For more rapid action, the intravenous preparations may be used. There is controversy over the use of ouabain, but Friedberg feels that it has the same margin of safety as digitalis. The dosage schedule is as follows:

| | Initial Dose | Onset of Action | Peak Action | Regression and Dissipation |
|---|---|---|---|---|
| Ouabain | 0.25 - 0.5 | 3 - 10 min. | ½ - 2 hr. | 12 hr. - 3 days |
| Acetyl Strophanthidin | 0.3 - 0.6 | 1 - 5 min. | 10 - 15 min. | 4 hr. |
| Lanatoside C | 0.8 | 10 - 30 min. | 1 - 3 hr. | 1 - 6 days |

Quinidine therapy is indicated when a return to normal sinus rhythm is desired. This is desirable when there is a history of previous arterial embolism, or when there is intractable heart failure. Contraindications are bundle branch block, or severe intraventricular conduction disturbance.

The dose of quinidine must be increased until the highest possible safe level is obtained. This is determined by symptoms, ECG, and if possible, by quinidine plasma concentrations. First a sensitivity test should be performed by giving one or two doses of 0.2 gm. an hour apart.

The dosage schedule is as follows:

| | | |
|---|---|---|
| Day 1 | 0.3 gm. | q2h x 6-8 |
| Day 2 | repeat | |
| Day 3 | 0.4 gm. | q2h x 6 |
| Day 4 | 0.6 gm. | q2h x 5 |
| Day 5 | 0.8 gm. | q2h x 5 |

The maintenance dose is approximately 0.4 gm. four times daily.

For more rapid action intramuscular administration is preferred. The dose is 4 mg. quinidine gluconate every 2 to 4 hours for one or two times.

Procaine amide may also be effective in converting atrial fibrillation to normal sinus rhythm. Digitalization should be performed first. The dosage schedule is 1 gm. orally every 3 to 4 hours for six doses. Usually a total dosage of 3 to 6 gm. is required. The drug should be lowered or discontinued in two weeks.

Anticoagulant therapy may be utilized in an attempt to prevent embolization due to the changing rhythm.

4. *Ventricular Tachycardia*

In ventricular tachycardia there is a rapid discharge of impulses from an ectopic focus of irritability in the ventrical musculature. The rate of discharge usually varies between 140 and 220 per minute. It usually occurs in paroxysms lasting for minutes or hours.

This condition is often associated with recent myocardial infarction. It may also occur with hypertensive, coronary, or rheumatic heart disease, and overdosage of digitalis, quinidine, or procaine amide.

The clinical forms are (1) terminal prefibrillatory tachycardia in association with seriously underlying disease (always fatal), (2) ventricular paroxysmal tachycardia due to a lesion of the septum, and (3) less serious forms occurring in apparently normal hearts.

Symptoms are attacks of palpitation with mild to moderate dypsnea, and dizziness and fainting.

On physical examination, the apical rate is from 160 to 180 per minute. Auscultation reveals irregularity in rhythm and cycle length, as well as variation in intensity of the first sound. The jugular "a" waves are fewer than the apical beats.

The ECG shows QRS complexes with approximately regular rhythm which are

slurred and widened. The rates vary from 150 to 200 per minute.

The treatment is (i) quinidine, with the same dosage schedule as under atrial fibrillation, or (ii) procaine amide given intravenously in 100 to 200 mg. doses per minute and up to a total of 2 gm. For slow infusions 1 to 2 gm. in 100 to 200 c.c. of 5% dextrose in water given at the rate of 3 cc. per minute. By intra-muscular route the initial dose is 0.5 to 1.0 gm. followed by 0.5 to 1.0 mgm. every four to six hours. Maintenance dosage is 0.5 gm. every four hours. (iii) Other agents include magnesium sulfate, calcium chloride, and potassium salts. For prophylaxis, quinidine is the drug of choice.

5. *Ventricular Fibrillation*

Ventricular fibrillation is defined as rapid irregular uncoordinated and ineffective twitchings of the ventricles. The mechanism is thought to be the same as that in atrial fibrillation.

It occurs following acute myocardial infarction, in the course of heart block with Adams-Stokes syndrome, after toxic doses of digitalis, and as a terminal event in a variety of diseases.

Clinically it presents as attacks of Adams-Stokes syndrome. Faintness occurs when ventricular fibrillation lasts three seconds or more, syncope after 10 to 20 seconds, and convulsions, apnea and incontinence after 40 seconds.

Treatment is the same as that of cardiac arrest. Immediate thoracotomy should be performed, and cardiac massage carried out. Oxygenation should be maintained by artificial respiration. Defibrillation can be attained by electric shock.

For paroxysms in a normal heart, quinidine or procaine amide may be used intramuscularly or intravenously. The dosage is the same as described under atrial fibrillation.

## SUMMARY

Certain arrhythmias can be identified by examination of the pulse rate and rhythm, or by cardiac auscultation. Occasionally asymptomatic arrhythmias are discovered accidentally. ECG is essential to the discovery and identification of other arrhythmias, especially the rhythm disturbances. Accurate diagnosis is especially rewarding in this field since specific effective therapy is available.

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# Ulcerative Colitis

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## INTRODUCTION

The disease entity known as ulcerative colitis is a chronic inflammatory reaction of the colon, of unknown etiology characterized by diffuse ulceration, watery mucoid stools, systemic manifestations, and periods of remission and exacerbation. It has been observed to be increasing in incidence in past years, occurring equally in male and female usually between the second and fourth decades. It is not, however, by any means unknown in children.

## ETIOLOGY AND PATHOGENESIS:

Since the exact cause of the disease is as yet unknown, many theories have been advanced as to its cause.

### 1. Lysozyme Theory:

It is known that lysozyme, a mucolytic enzyme, is produced by the colonic mucosa, this product appearing to be under nervous control. Huge amounts have been found in the stools of persons suffering with the disease. This enzyme is thought to liquefy the mucus which normally protects the mucosa from the action of bacteria and proteolytic enzymes found normally in the stool.

Because of the high concentration of the enzymes in the stools of persons prone to or suffering from the disease, lysozyme has been considered as the causative agent by some investigators though the course of the disease remains unaltered by the administration of antilysozymic agents.

### 2. Psychic Theory:

Emotional upsets seem to play an important part in the etiology. Frequently feelings of resentment and anxiety are associated with exacerbations. (The proponents of the lysozyme theory feel that these emotional upsets trigger the production of lysozyme which in turn causes the exacerbation). It is theorized that these psychic upsets result in nervous impulses being sent to the colon which cause vascular, motor and secretory abnormalities rendering the mucosa more susceptible to invasion by bowel bacteria or to digestion by enzymes in the stool (trypsin). There has however been no evidence to support this hypothesis, nor does there seem to be any particular personality type predisposing to the disease.

### 3. Collagen Theory:

Some physicians feel ulcerative colitis should be classed as a collagen disease. They cite as evidence the systemic nature of the disease, the associated arthritis and erythema nodosum-like lesions, the inflammatory reaction of the submucosa and the changes in the ground substance of the mucosal basement membrane.

### 4. Stress Theory:

Still others feel that the condition may be a non-specific type of reaction to various types of injury, the types of injury being trauma, psychogenic upset, or infection elsewhere in the body. They think that perhaps the colon of certain persons is hyper-reactive to such injury with the resulting pathology.

5. **Other theories**, such as allergy, deficiency and specific causative organism the-

ories, have been proposed but lack supportive evidence.

## PATHOLOGY

The lesions usually commence in the rectum and sigmoid colon and then proceed toward the splenic flexure. In severe cases, the whole of the large bowel may be affected with extension of the disease process into the terminal ilium.

The colonic mucosa is eroded by multiple variable-sized ulcers which may coalesce to form irregular bands. These ulcers may extend completely through the muscularis mucosa so that the ulcer base lies on the peritoneal surface of the bowel. The mucosa surviving between the ulcers is swollen and edematous, giving a polypoid appearance to the bowel. As the disease progresses, ulceration increases, leaving whole areas denuded. The wall of the colon may become quite friable and the mesenteric lymph nodes often are enlarged and tender.

Microscopically, the ulcerated areas show thickened submucosa infiltrated with lymphocytes and chronic inflammatory cells. The muscularis also shows an inflammatory reaction. The surviving areas of mucosa become hyperplastic and edematous. The ulcerated areas heal in time by fibrosis which may produce some stenosis of the lumen. Occasionally an ulcer may penetrate the wall and cause thickening of the overlying serosa.

## CLINICAL MANIFESTATIONS

Varying degrees of signs and symptoms may be present depending upon the stage and rate of progression of the particular case.

### Symptoms

The onset is usually insidious in nature but may be acute. Ulcerative colitis tends to run a chronic progressive course with acute exacerbations. Rarely a fulminating case may be seen.

Blood and mucus in the stool is a major symptom. The blood, mucus and pus, if present, are mixed through the stool, producing bright red streaking. The stools are never tarry. At times, when the disease seems to be quiescent, gross blood may not be apparent. Bowel irregularity may be noticed for months or years prior to the onset of the disease. The patient has a desire to defecate frequently. This increases in frequency as the disease progresses and it is not uncommon to see fifteen to thirty bowel movements per day in an acute exacerbation. In cases with severe diarrhea, much loss of body fluids may occur.

Abdominal discomfort is usual but abdominal pain is rare. When pain is present it is of colicky nature, present prior to a bowel movement and relieved by a bowel movement. Severe crampy abdominal pain may occur with a fulminating type of disease.

Rectal tenesmus may occur if the rectum is involved in the ulcerative process.

General malaise, anorexia and weight loss are prominent in the course of the disease, especially in the more acute forms.

Symptoms of anemia may be evident if sufficient blood has been lost (i.e., pallor, palpitation, weakness and fatigue). If the anemia is sufficiently severe, ascites and edema of the ankles may appear.

In mild cases, the patient often feels so well that co-operation in therapy is often difficult to attain.

### Signs

A low grade fever, irregular in nature, and often present in the evening, is present in the chronic type of disease, a manifestation of the toxemia.

Abdominal tenderness is present rarely and only if the inflammatory process has spread to the peritoneum and a local peritonitis has appeared. Abdominal rigidity

then may be present. Abdominal distention occurs only in severe cases.

Rectal digital examination usually reveals nothing. Pain may be present if the rectum is ulcerated and blood may be noticed on the examining finger when it is withdrawn.

Signs of dehydration may become evident in cases with severe diarrhea and fluid loss.

## DIAGNOSIS

### A. History and Physical Examination

A carefully taken and intelligently considered history and physical examination is important in the diagnosis of the disease. Signs and symptoms discussed above must be looked for, especially those of blood and pus in the feces and the extreme frequency of bowel movements.

### B. Laboratory Procedures

1. Urinalysis is usually normal.

2. Hematological studies will show a mild neutrophilic leucocytosis and an increased erythrocyte sedimentation rate (ESR). A hypochromic microcytic anemia is present if sufficient blood has been lost in the stools.

Hypoproteinemia is the most important blood chemical change. It is due to loss of protein in the stool, decreased intake, or the decreased ability of the liver to form plasma protein. In severe cases, the prothrombin time is increased due to loss of vitamin K in the stool.

3. *Examination of feces* is necessary for both diagnosis and prognosis in ulcerative colitis. The presence of mucus, blood and pus should be noted both grossly and microscopically. As the patient improves, these decrease in amount in the stool.

The stool should be examined for the following organisms:

(i) Entameba histolytica, (ii) dysentery bacilli, (iii) acid-fast organisms. To detect the presence of tubercule bacilli, a formalin-prepared specimen is required. A smear may be made and studied for these organisms.

Culture of material collected from an ulcerated area on sigmoidoscopic examination may be very useful in eliminating entameba histolytica or shigella.

### C. Special Diagnostic Procedures

1. *Sigmoidoscopic examination* must be performed with care in view of the possibility of causing rupture or hemorrhage. The findings vary with the extent of the disease.

In the acute stage, the mucosa is edematous, diffusely granular, friable and coated with mucus. Many superficial bleeding points are visible. As the disease progresses ulceration becomes quite evident and a thick mucopurulent secretion coats the colon. The ulcers bleed very easily when touched.

In the chronic stage, the mucosa appears thickened, pale, firm, and granular with loss of normal mucosal architecture. The lumen may or may not be narrowed. Pseudopolyps may be seen in the sigmoid or rectum.

2. *Roentgenologic examination of the colon* using a barium enema reveals characteristic changes which are, however, first evident much later than those seen with the sigmoidoscope. Early in the disease there may be no change evident.

The first change noticed is the sawtooth appearance of the colon due to hyperirritability of the colon. Later the normal mucosal pattern is lost, becoming quite irregular and distorted. Filling defects may be noted, these being due to epithelial polypoid hyperplasia. The changes in the final stages of the disease are replacement of the normal haustrations by a smooth, regular, "lead pipe" picture with the diameter of the lumen considerably narrowed.

## DIFFERENTIAL DIAGNOSIS

Ulcerative colitis may simulate many other disturbances of the bowel, the more important of which are described below.

1. *Amebiasis or amoebic dysentery* may be differentiated by feces culture or by examination of the material obtained by rectal swab for the specific ameba. Sigmoidoscopic examination of the intestinal mucosa will reveal sharply punched out irregular ulcers scattered over the otherwise normal mucosa.

2. *Bacillary dysentery,* caused by the shigella organism, is differentiated by the demonstration of the specific organism on culture of feces or by examination of a smear of material obtained by rectal swab.

3. *Tuberculous enteritis* usually involves the cecum and ascending colon. It is usually, in these days, associated with a form of tuberculosis elsewhere in the body (usually pulmonary).

4. *Malignant disease of rectum, sigmoid and colon* are usually identified by radiological examination, sigmoidoscopic examination, history and physical findings. These diseases occur in older age groups and rarely cause purulent rectal discharge.

5. *Regional enteritis or ileitis (Crohn's disease)* commonly has a characteristic X-ray picture. It shows normal mucosa on sigmoidoscopic examination. Gross blood is less likely to occur in the stool.

6. *Staphylococcal enterocolitis* may be suggested if there is an associated history of antibiotic therapy.

7. *Uremic colitis* occurs only in association with renal failure.

8. *Diverticulitis* occurs in an older age group than the one in ulcerative colitis. It may be readily diagnosed on radiological examination of the large bowel.

9. *Lymphopathia venereum* is identical to ulcerative colitis on sigmoidoscopic examination. There is however a history of inguinal adenopathy and a female preponderance. A positive Frei Test, hyperglobulinemia, and the presence of a rectal stricture gives further support to this diagnosis.

## TREATMENT

Treatment when initiated has one of two objectives, (a) to prepare the patient for surgery or (b) to maintain the patient through the course of his disease by means of conservative medical management. There is however no specific curative therapy. Patience and perseverance by both patient and physician form the basis of successful maintenance therapy.

### A. Prophylaxis

There are no prophylactic measures known to prevent the disease, but in a known case the prevention of acute emotional stress may assist in preventing an exacerbation of the disease.

### B. Medical Management

1. Total bed rest, usually in hospital, is absolutely essential in an acute exacerbation. Rest should be continued until the pyrexia has subsided and the bowel movements have decreased to 3 or 4 each day. Gradual return to activity is then begun. Phenobarbital (gr. ½ t.i.d. and gr. 1½ h.s.) will help attain the desired rest.

2. A diet high in calories, proteins, minerals and vitamins should be prescribed. The patient must be encouraged to eat a full diet. The more severe cases may not be able to tolerate this diet and may as a result pass into negative nitrogen balance. These patients must be maintained on transfusions of blood plasma or dextrose until food can be tolerated. Fluid and electrolyte loss, especially loss of potassium and chlorides, must be corrected by means of intravenous infusion.

3. Cortisone or adrenocorticotrophic hormone therapy has made a great advance in the treatment of ulcerative colitis. This

therapy is not curative but only serves to induce remission. The indications for its use are:

(a) acute fulminating disease,

(b) acute exacerbations of chronic disease,

(c) preparation for surgery,

(d) long-term maintenance therapy in chronic intractable disease.

Less benefit is derived from the drug if complications have developed. The remissions produced by its use are not permanent. Cortisone is thought to be the best of the corticosteroids as there will probably be less tendency for the colon to perforate. Large doses (200 mg. daily) are used and accompanied by supplements of potassium salts. This therapy may have to be carried on longer than desired and salt retention and edema will develop. Diuretics are given to combat the complication of edema. The drug gives the patient a sense of well being and an increased desire for food.

4. Nitropine sulfate (0.6-1.0 mg. q.i.d.) or belladona (10-30 drops q.i.d.) is used to decrease the motility of the intestine. If excessive diarrhea persists, codeine or tincture of opium can be used.

5. Sulfonamides or antibiotics do not alter the course of the disease but will prevent a secondary bacterial infection. Gantrisin (4 to 6 gm./day) is the drug used most frequently. If a perforation has occurred a combination of antibiotics is used (penicillin and streptomycin).

6. A patient with this disease is quite upset emotionally and reassurance and confidence supplied by the attending physician is very important. The physician must try to return the patient to as normal a way of life as possible in the shortest time possible.

### C. Surgery

Medical therapy has been effective in controlling fifty to eighty per cent of the patients. In the other cases surgical intervention is necessary. The decision for surgery can be a difficult problem, but in general the indications are:

1. Perforation of the bowel.
2. Presence of stricture, especially rectal stricture.
3. Cases of polyposis where danger of malignant change is present.
4. Perianal abscess and fistula.
5. Intractable diarrhea, anemia, and malnutrition.
6. Recurrent massive hemorrhage.
7. Arthritis and Pyoderma gangrenosum.
8. Malignant changes.

The surgical intervention in fulminating ulcerative colitis has been disappointing. An emergency operation is not necessary. The patient should be brought to the best possible condition before the operation is performed. The surgical treatment of choice is a total or subtotal colectomy with a permanent ileostomy performed in one stage. If the disease has spread to the rectum an abdominoperineal resection is done also. Older operations of vagotomy, cecostomy, and internal defunctioning anastomoses have disappeared from use. The problem of the operation used now is a prolapse of the ileum at the connection to the skin. No technique so far developed has prevented this. Bowel obstruction or electrolyte imbalance may complicate the latter temporarily.

## COMPLICATIONS

Numerous complications may develop from this disease but the major ones are:

1. Pseudopolyposis formation with a greater tendency to malignant change.
2. Stricture formation which may lead to intestinal obstruction.
3. Perirectal abscess, a source of great pain and discomfort.

4. Fistula formation.

5. Perforation with peritonitis.

6. Malignant change. Five to ten per cent of patients with ulcerative colitis develop colonic cancer.

A few minor complications are:

1. Hemorrhoids.

2. Anal fissures.

3. Pruritus.

4. Hypertrophic osteoarthropathy.

## PROGNOSIS

The outcome of an individual case seems to be quite uncertain and, therefore, the statement of a prognosis should be guarded. The prognosis seems to be worse in a young individual or a patient with fulminating disease. The greater the amount of colon affected with the disease process, the worse is the prognosis. The overall surgical and medical mortality is 10%. Good results can be expected in 65 to 75% of the cases carried on medical management.

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# Abstracts

## A RATIONAL APPROACH TO ANTIBIOTIC THERAPY OF CHILDHOOD INFECTIONS

C. Henry Kempe, Post Grad. Med. J., 24: 325-341, 1958

The indiscriminant use of antibiotics for fevers and diseases of unknown origins has resulted in the masking of serious illnesses and the evolution of many more drug-resistant bacteria.

When administering antibiotics to any patient the doctor should ask himself the following questions:

1. Is this a bacterial disease and if so, which one?
2. Where are the majority of the bacteria?
3. What route of administration of the drug will produce the best results?

Bacterial complications in pediatric surgery are five times commoner in patients who are given antibiotics prophylactically than in control groups. When the susceptible organisms are removed, the remaining ones quickly multiply and become pathogenic.

Included are three tables listing the pediatric dosages of the common antibiotics, the anti-microbial spectra of these drugs and their toxic effects.

The important features of some of the common antibiotics are:

1. Polymixin B is the only drug which is useful in the treatment of Pseudomonas aeroginosa infections. It is absorbed poorly from the gastro-intestinal tract and is therefore of no use in systemic infections when given orally.

2. Bacitracin is one of the more useful drugs in treating penicillin-resistant organisms. Its action is often synergistic to that of penicillin and streptomycin. Administration should not be prolonged in view of its toxic side effects.

3. Neomycin is effective against both gram-positive and gram-negative bacteria but with its use come certain undesirable side effects. It has caused deafness and irreversible renal damage when used in large dosages for a prolonged period. Oral administration to infants and patients with ulcerative colitis may result in systemic absorption and severe toxicity.

4. Erythromycin is the drug of choice for diphtheria, prevention of rheumatic fever, penicillin - resistant staphylococci, and for patients sensitive to penicillin.

5. Novobiocin sensitization has developed in at least 35% of all children treated with the drug. It is therefore inadvisable to use it except for treatment of resistant staphylococcal and proteus infections.

6. Ristocetin is used only for penicillin-resistant staphylococci in which the intravenous route of administration is justified.

When combinations of antibiotics are desired the physician should provide for them in his own way and base his combinations on his own judgement because many of the commercial preparations are effective only in adults. Indications for drug combinations are:

1. Mixed infections.
2. Prevention of emergence of drug-resistant mutants.
3. Desirability of additive synergistic effects.

Long term tetracycline prophylaxis is the physician's responsibility in rheumatic fever, post-streptococcal glomerulonephritis, fibrocystic disease, agammaglobulinemia, steroid therapy and other conditions subject to frequent bacterial infections.

Hospitals in Colorado have found that the restriction of the use of penicillin for a 6 month period has resulted in an increased usefulness of penicillin in the treatment of staphylococcal infections which had been almost totally penicillin-resistant.

—Glenn Oliver, '60

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